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MPV And DENGUE

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Abstract: ***Dengue virus results in myriad of clinical states: from asymptomatic to severe symptomatic disease. The later state is often a 'dynamic' process, ranging from self limiting dengue fever (DF) to severe dengue. Severe dengue manifests either as bleeding (dengue haemorrhagic fever, DHF), hypovolemic shock (dengue shock syndrome, DSS) or severe organ impairment. Bleeding is resultant to microangiopathy and thrombocytopenia (TCP); shock due to capillary plasma leakage; organ failure representing shock or microangiopathy associated hypoxic. TCP a common element in dengue fever and severe dengue, is worrisome to clinicians who have a tendency to 'react' to TCP via platelet transfusions. Readily available lab parameters to guide the clinician of platelet recovery is needed. One such parameter gaining recent interest is Platelet Indices (PIs): MPV and PDW, we believe serially observing the MPV and Platelets might be a useful, with a rising trend in MPV heralding platelet and patient recover.***

I. BACKGROUND

Platelets indices are relatively new knowledge in clinical practice, and its use is not optimal and is still being defined. It has been proposed as having a value in disease course of various infectious and noninfectious entities. In Dengue Fever (DF) it has been emphasised to have value in diagnosing and classifying into Dengue Fever (DF) or Severe Dengue. The principal financial burden in dengue management is platelet transfusions, a single transfusion costs around 12,000 Indian rupees (INR), around 200 USD, in fact, the economic burden of 2006 Dengue epidemic in Delhi was close to 27.4 million (USD). A tendency for 'platelet chasing' and resultant platelet transfusion has been noted in Indian circumstance, the so called 'Dengue Panic Syndrome". Lab parameters to guide the clinician of an impending TCP recovery is needed; Immature platelet fraction (IPF) estimation has been proposed to predict recovery and outcome, unfortunately it is not available with all semiautomatic analysers. The readily available PIs: Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), reported by most automatic, semiautomatic cell counters may serve as a useful guide.

II. CLINICAL PRESENTATION

31 year old female with dengue fever, hypotension and TCP (Severe Dengue) was referred to our unit for platelet transfusion, she was managed on lines of 'typhoid-malaria' since last one week by village level practitioners many of whom are educated till primary school level or less. Later she was investigated routinely as she reported 'not feeling well' with persistent nausea and vomiting (Dengue warning signs) and found to have platelets alarmingly low—19,000; Dengue NS1 rapid card test positive. At presentation she complained of vaginal bleeding, without any petechia or tourniquet test positivity, she had her last cycle 12 days back, and had no irregular menstrual history. On examination her Pulse was 98, BP was 96/80, afebrile, SP02 -98 on ambient air, on auscultation of chest bilateral air entry without added sounds, Heart sounds were audible without any murmurs, she was not in any distress, higher mental functions were intact.

III. LAB EVALUATION

Her initial Complete blood count (CBP) showed Haemoglobin (Hb)-13.0, hematocrit (HCT)-39, Platelet count -19,000, Total Counts-6,600, Transaminases (AST and ALTs) mildly raised to 56 and 60 respectively, other routine

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parameters viz., electrolytes renal function were normal, Chest Xray Postero-anterior-view (CXR-PA View) and USG abdomen were normal without any evidence of ascites or plural fluid.. Complete urine examination (CUE) showed pH 6, Specific Gravity 1015, no glycosuria, proteinuria 1+, no ketones, Bilirubin 1+, PT and aPTT were found to be normal. Dengue Rapid Diagnostic Kit Test (Jay Mitra) showed Non Structural Protein 1 antigen test (NS1) and IgM positive, IgG negative.

IV. TREATMENT

She was started on fluids and other supportive measures. As she had vaginal bleeding, Pulse Pressure at 16 (BP was 96/80) a consideration for Platelet transfusion was deferred, considering the possibility of manifestation of leakage after fluid infusions she was on close observation.

V. OUTCOME AND FOLLOWUP

Her general condition improved with simple measure of hydration and she made an uneventful recovery. During the course of her recovery her Platelet indices (PIs) viz., MPV, PDW suggested a pattern: at initial evaluation MPV was 9, PDW-14, a comparison from her village lab report was not possible as the analyser printout was not attached and the only reported PIs was the platelet count. The next morning although her vaginal bleeding continued the platelet count improved to 26,000 with MPV-10.1, PDW-18.2, and HCT-40.3, fluids were continued and she remained stable. Further trend in her PIs during the course of hospital stay are tabulated below:

DAY OF HOSPITALISATION	PLATELETS	MPV	PDW
DAY 1	**26,000**	9	14
DAY 2	**29,000**	10.1	18.2
DAY 3	**31,000**	11.8	22.4
DAY 4	**40,000**	11.1	26.6
DAY 5	**61,000**	14.2	30.8

Table 1

VI. DISCUSSION

A trend of considering all fever as typhoid, malaria and 'typhoid malaria' is common in resource limited setups of rural India, another unfortunate trend is reporting of only basic haematological parameters in CBP report, as most clinicians are unaware of any clinical importance of 'extended parameters' they hardly insist for a complete report or a analyser printout which contains the complete parameters. This patient had the tell-tale evidence of such an approach.

In view of a possible pattern in her PIs, a thorough review of literature was initiated, it has been reported that the mean MPV in south Indian females is 10.1. Bashir et al., have reported that MPV has a tendency to fall in the initial stages of DF and MPV <9 having considerable sensitivity (>90%) for dengue fever. This patients MPV of 9 on Day 1 thus allows the clinician to consider DF, an earlier labs record would have been more helpful to know what was her nadir MPV, unfortunately it was not reported, depriving the clinician of an important clue. Furthermore, her MPV improved the next day to 10.1 and subsequently more robustly, paralleling her general recovery and improvement in haematological parameters.

The correlation coefficient (R) of MPV and Platelets was 0.9 suggesting a strong positive correlation. A similar trend albeit modest is observed in Prakash et al., study where in the MPV and Platelet counts is correlated for 3 days on the third day of evaluation an r value of 0.45 is observed suggesting moderate correlation. But, on day 1 and day 2 of their study an r-value of 0.159 and 0.214 was noted suggesting no correlation or very minimal correlation. However a trend of correlation strength over the 3 days in their study is hard to miss.

The pathogenesis of thrombocytopenia in dengue is not fully known, with two major hypotheses: first, decreased production resultant to bone marrow depression by dengue virus, second, immune (anti-dengue antibodies/immune complex) mediated destruction of platelets, 11 of 61 patients studied by Mitrakul et al., had destruction as a main cause for TCP as revealed by platelet kinetic study. Furthermore, low grade inflammatory disorders result in platelet activation and rise in MPV, in contrast high grade inflammatory disorders have consumption of large platelets at the inflammation site and result in decreased MPV. But, inflammatory process causing significant MPV alteration seems unlikely in many Dengue patients. Thus, a low MPV implies marrow suppression as a cause of thrombocytopenia and a rising MPV heralds the improvement in platelet count, as was observed in our patient. In fact, a low MPV in Indian subset of patients been reported in more than two third of the Navya et al study group DF patients. Other studies didn't find consistent correlation with MPV and Dengue severity, that might be partly due to different pathogenesis or lack of a similar design to observe the MPV and Platelets serially till recovery.

Serially observing the MPV and platelets may guide a clinician in an important subset of patients in DF and severe dengue where the mechanism of TCP is largely marrow suppression—initial MPV significantly low and the TCP recovery following the MPV. However in patients with immune mediated destruction, or other hitherto unknown mechanisms as the cause of TCP a rising MPV may not immediately suggest a possible recovery as the insult is on going, but even then the robustness of marrow response depicted by an increasing MPV might imply good outcome. More studies to this end are definitely needed, as these parameters are available for analysis at no additional cost. Goethe said, "man sieht nur das, was man weiß" (You only see what you know). Time to see.

PATIENT'S PERSPECTIVE

I was initially informed by my village practitioner for urgent need of 'Platelet transfusion' without which I may not survive the illness, knowing the financial difficulty I feared the worst.

I thank my doctors who took a thoughtful approach and waited it out, I had an uneventful recovery.

LEARNING POINTS

The Chasing of platelet in DF has to be avoided, a minor bleeding event with slight decrease in Pulse pressure, a minimal hypotension and a platelet <20,000 (all a manifestation of severe dengue) is not a reason to panic and transfuse platelets.

Decreased MPV in the setting of DF and DHF may imply marrow suppression and increasing MPV can predict recovery in these subset of patients.

Platelet destruction (immune mediated) is reflected as a cause if rising MPV is associated with ongoing TCP, in this subset, MPV may not predict expected recovery.

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